the distinguishing language introduced by the amendment of claim 32 added new matter and hence may be disregarded. These claims are also rejected as anticipated by Dengrove (§8), Halsey (§9), and John (§10).

The Examiner is respectfully reminded that the amendment of claim 32 was made prior to final rejection and hence its entry was a matter of right. We know of no legal authority which says that a claim limitation material to patentability (§§102, 103) may be disregarded because the Examiner has some other criticism of it. As stated in MPEP §706.03(o), "New Matter", In the "Examiner's note" on page 700-38, while adding "new matter" to a claim warrants a rejection under the description requirement of 35 USC §112, para. 1, see form para. 7.31.01 on page 700-34, as to any prior art issue, "the new matter must be considered part of the claimed subject matter and cannot be ignored". If the Examiner is found to be correct that the limitation in question is "new matter", and the limitation is cancelled, without replacement with some other distinguishing limitation, the PTO may at that time reject the claim over the art. Until then, the claim must be read as it is written, and the rejection withdrawn.

The last amendment explains in detail how Madore, Dengrove, John, and Halsey are distinguished by claim 32 as amended. The Examiner has not challenged the accuracy of this explanation.

2.2. It is noted for the record that method claims 56-58 have apparently been conceded to be free of the prior art.

2.3. The Examiner maintains the rejection of the kit claims as anticipated by Madore (§7), Dengrove (§8), Halsey (§9), John (§10) and Onazono (§11) on the ground that there allegedly is not functional relationship between the printed matter and its substrate, as required by In re Gulack, 217 USPQ 401 (Fed. Cir. 1983) and In re Muller, 164 USPQ 46 (CCPA 1969).

What is a "functional relationship"? Presumably, it implies that without the printed matter, the substrate would be less capable of performing its function.

In the case of In re Miller, claim 10 read as follows:

> A measuring device comprising: a spoon for measuring ingredients; and volume measuring indicia defined in a normal volumetric unit on said spoon of a selected ratio to but indicating a volume different from the actual volume of ingredients being added to and measured in said spoon by said indicia, and a legend attached to said spoon specifying said ratio.

The court's opinion reproduces two apparatus of this type. In Fig. 2, we see a measuring cup with the legend "ONE HALF RECIPE", and various volumetric indicia. The line marked "2 CUPS" actually corresponds to a volume of one cup, so, if a full recipe called for "2 cups", by filling to the line in question, one would actually be adding the amount appropriate for a half recipe. In Fig. 3, we see a set of measuring spoons with a "1/2 recipe" tag. Here, the spoon marked "1 teaspoon" has a true capacity of 1/2 teaspoon.

Were these indicia and legends to be removed, one would have cups and spoons worthless for accurate measurement. If just the legends were removed, one would have just a conventional looking (but inaccurate) measuring device or cup. The Court found that there was "a new and unobvious functional relationship between a measuring receptacle, volumetric indicia thereon indicating volume in a certain ratio to actual volume, and a legend indicating the ratio".

Similarly, in the instant kit claims, there is a new and unobvious relationship among "containers holding pharmaceutically acceptable doses of one or more immunogens" (which is like Miller's "receptacle") the "labeling" of the containers to indicate the identity and amount of each immunogen they contain (which is like Miller's "volumetric indicia")[2] and the "instructions" for use (which is like Miller's "legend").

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[2] While this is not explicit in claims 27 and 29, it is an FDA requirement. The Supplemental Amendment, if entered, would make this explicit.

The last of these points deserves particular emphasis. Miller's "legend" is an instruction for use. "One Half Recipe" is an instruction to the cook to use the cup or spoon se tin question when he or she wishes to prepare a "one half" recipe without recomputation of the required amount of each ingredient. Without the cook to interpret the legends and indicia, the cup and spoons do not perform any function. Their functionality resides in what they communicate to the cook. They do not help the receptacle hold more ingredients, or keep them fresher. They do not make the receptacle more watertight or airtight. Their relationship -- especially the legend's relationship -- to the receptacle is closely akin to the relationship exhibited by the printed matter in the instant kit claims to the immunogens of those claims.

In Gulack, the claim was to an educational device, which could take the form of a hat with a headband. Imprinted on the headband (the substrate) was a cyclic sequence of integers (the printed matter) obeying a particular mathematical rule. What was the functional relationship? According to the CCPA, the digits -- the printed matter -- were "related to the band in two ways: (1) the band supports the digits; and (2) there is an endless sequence of digits... exploit[ing] the endless nature of the band". In contrast, in the prior art Wittcoff reference, there was printed matter on the band, as in (1) above, but the data items were independent rather than arranged in a particular sequence.

Here, the labeling establishes a sequence, albeit temporal rather than spatial, for the use of the immunogens of the kit. Bear in mind that this relationship is between the printed matter and the immunogens, which are a part of the overall "substrate". In Gulack, the distinguishing relationship was between one printed element and another printed element. Hence, the present case actually presents a stronger justification for the finding of a functional relationship than does Gulack.

Consistent with this analysis, the PTO has allowed claims

with "labeling" limitations.

Gerbe, USP 3,627,122, SYSTEM AND APPARATUS FOR THE ADMINISTRATION OF DRUGS (1971), claims an apparatus comprising compartmented trays, with "a patient and dose identification card" covering the bottom of each compartment, the card "having a folded portion...for holding said card in place". The claim also recites that each compartment has "a longitudinal pocket in one wall for a signal identification card".

Phykitt, USP 5,687,841, COMBINATION SHIPPING CONTAINER, MIXING AND DRINKING VESSEL (1997) claims the combination of analgesic medications and a package which serves both a shipping container and a mixing vessel. Claims 21-22 recite

> 21. The combination, according to claim 1, wherein said package further includes at least one of indications, directions, warnings, drug interaction precautions, active ingredients information and storage information disposed on an outer surface of one of said back portion and said front portion of said package.
>
> 22. The combination, according to claim 21, wherein said package includes each of said indications, said directions, said warnings, said drug interaction precautions, said active ingredients information and said storage information disposed on said outer portion of said back portion of said package.

Robertson, USP 5,752,723, PHARMACY LABEL AND PRESCRIPTION DRUG DISPENSING (1988) claims (18) "a labeled prescription drug package comprising...indicia comprising the name of a prescription drug, the dosage for proper administration of the drug, and the quantity of the drug to be provided in a package, imaged on said first label section".

See also Olney, USP 5,011,853 (claim 18= "a label which indicates that said pharmaceutical agent can be used for reducing the neurotoxicity of at least one cholinergic neurotoxin"); Kelly, USP 5,208,031 (claim 4= "the packaging material indicates that the sexual lubricant mixture... can reduce the risk of being

infected by at least one type of sexually transmitted virus"); Sanders USP 4,820,635 (claim 1= "A kit ...comprising... instructions for performing the assay").

The purpose of the patent system is to encourage innovation. The claims are a means of defining the invention in such a manner that it is reasonably clear what has been patented. It is one thing to reject a claim because it covers subject matter which is disclosed or suggested by the prior art, or which is not enabled. It is quite another to reject it on what amounts to stylistic grounds.

The PTO and the courts have recognized the propriety of once exotic claim formats-- "Jepson" claims, "Markush" claims, "product-by-process" claims, "fingerprint" claims, and claims with "negative", "functional", or "alternative' limitations -- because they have realized that public policy demands that inventors not be hindered by hypertechnical claim drafting rules from fully protecting novel, nonobvious, and adequately disclosed inventions.

The instant "kit" claims are a case in point. Applicant has discovered that immunization can --depending on timing - either increase or decrease the incidence or severity of chronic immune-mediated disorders such as diabetes and SLE. A traditional product claim does not sufficiently protect applicant, as it cannot cover a prior art vaccine, even if that vaccine were used without consideration of its effect on a chronic immune-mediated disorder.

For a method claim to protect the invention, it must be crafted to avoid any instance in which the prior art use of a vaccine to immunize against an infectious disease might inherently (although inadvertently) have had the effect of also reducing the incidence or severity of a chronic immune-mediated disorder, as otherwise it could be held invalid on the ground of "inherent anticipation". Applicant has studied the literature, and has attempted to phrase the claim so as to avoid inherent anticipation, but simply cannot be sure that all such art has

been avoided. An early immunization protocol might be set forth in an old or obscure journal anywhere in the world, or might have been used "publicly", without formal publication, in the United States. Indeed, the specification at page 31, lines 9-18 expressly recognizes the problem:

> The inventor appreciates that it is conceivable that a prior experimenter has, without recognition of its anti-chronic immune-mediated disorder activity, proposed or even practiced an immunization schedule which falls within the present disclosure, If, under the applicable law, such a proposal or practice would be deemed to anticipate or render obvious an invention here claimed, then it is within the inventor's contemplation to excise from the invention the specific embodiment in question, preserving to the maximum degree permitted by law the scope of protection originally sought.

A second problem with method claim protection is that it is geared to use of immunogens to decrease the incidence or severity of a chronic immune-mediated disorder. However, the Applicant has also enriched the art by teaching it to examine the chronic immune effects of conventional immunization. A vaccine manufacturer may find, after testing inspired by Applicant, that early immunization, while less likely to elicit this adverse effect, is also less effective against the infectious disease, and therefore continue to recommend, with appropriate warnings, late immunization. A "method of reducing the incidence or severity of a chronic immune-mediated disorder" claim would not reach this practice, even though the manufacturer would clearly have benefitted from Applicants's teachings.

A third problem is that the method claims are infringed by physicians. Applicant would prefer to assert direct infringement by the manufacturer. It is easier for Applicant to monitor vaccine labeling than to identify which doctors are following the claimed early immunization strategies.

A "kit" claim, like claims 27 and 59, solve these problems, without giving Applicant control of subject matter to which he

is not entitled. Claim 27 and 59 are infringed only if the immunogen is distributed or sold with labeling either giving instructions which call upon the physician to practice the invention, or warnings indicating that the manufacturer has screened the immunogen as taught by Applicant.

Claims 27 and 59 could not be inherently anticipated by the naive use of the immunogen in an early immunization schedule, since such use, by definition, would make no reference to the effect of the immunogen on the incidence or severity of a chronic immune-mediated disorder.

3. Definiteness

1. The rejection vis-a-vis "pediatric" and "nonpediatric" has been withdrawn (sec. 5(b)).

2. With regard to "substantially" (secs. 5(a) and (c)), the question raised by the Examiner --how much greater is "substantially greater" -- was also asked by the Examiner in In re Mattison, 184 USPQ 485 (CCPA 1975). The Court reversed the rejection, saying that it was not necessary to fix it as being 5%, 50% or 500% greater.

3. In section 5(d), the Examiner appears to be arguing that "immunogen other than BCG" is indefinite because "immunogen" per se is indefinite. The term "immunogen" is formally defined at page 33, line 19 to page 34, line 2. Numerous examples are given on pages 35-36, and the term is widely used in the art. Also, the specification formally distinguishes immunosuppressants (defined at page 36, lines 16-18), tolerogens (defined at page 36, lines 20-23), immunocyte receptor ligands (page 37, lines 9-12), anti-receptor molecules (page 39, lines 12-21), transplanted cells (page 39, lines 22-29), and general immune modulators (page 40, lines 1-18).

4. In section 5(e), the Examiner criticizes "specific times after birth". The Examiner fails to understand the difference between a broad limitation and an indefinite one. Which term is unclear? An administration can only be before birth, at birth,

or after birth. "Specific times" excludes continuous administration, and also implies more than one discrete administration.

Claim 31, whether the language originally appeared, was cancelled. In claim 56, the "specific times" are actually specified further in lines 10-12 and 19-25. Likewise, in claim 32, the times are limited to those set forth in lines 10-12, 15-17 and 21-26.

Upon review, it appears that, in claims 32 and 56 at least, the phrase is surplusage, and hence it has been deleted from those claims.

4. New Matter/Description

Claims 6, 32 and 101 have been rejected (OA, Section 12) because the added limitations allegedly do not satisfy the description requirement, i.e., they were not part of the original conception of the rejection.

Claim 6 is rejected solely because it is now dependent on claim 32. The same appears to be true of claim 101, since it is not separately argued and the immune response it envisions would appear to be inherent in the immunization against an infectious disease contemplated by original claim 31. Hence, the rejection hinges on claim 32.

Claim 32 was amended to add three limitations.

(1) if only one immunogen is administered, it is other than BCG;

(2) if the one immunogen is whole cell pertussis, the schedule is one other than a schedule of three doses at one week intervals, all given in the first month; and

(3) if all the immunogens administered are selected from a list of 10 immunogens, either

(a) one or more immunogens are administered on at least three different dates prior to 42 days after

> birth, or (b) one or more immunogens are administered on at least three different dates, and the maximum interval between administrations is about two weeks, or less.

We explained on page 11, lines 2-27 of the last amendment:

> Limitations (1) and (3) are copied from claim 1 of Classen, USP 5,728,385, which issued on the parent application, except that claim 32 refers to "one or more immunogens" instead of just "immunogens" to make it clear that a single immunogen could be administered. Note that the immunogens administered on different dates could be the same or different.
>
> Limitation (2) is introduced to avoid any possibility of inherent anticipation by Adams (1947) (copy enclosed)[3], as cited in Table 5 of Halsey (of record). Excission of a prior art species from a generic claim is proper, see In re Johnson, 194 USPQ 187 (CCPA 1977) and indeed was contemplated as a possibility, see page 31, lines 9-18. The Halsey article is cited in the specification (p. 109) and incorporated by reference, as are all articles (including Adams) cited by Halsey. See pp. 99-100. Hence, there is no violation of the "description" requirement.

The Examiner says that because this case is a CIP of the prior case, and does not incorporate the prior case by reference, he cannot assume that just because there was descriptive basis in the parent case (as implied by the issuance of a patent) that there is descriptive basis here.

In terms of justifying the limitations on the basis of the present specification, we have already explained the basis for limitation (2). However, we would add that there is specific support for giving at least three doses (original claims 9, 12 and 13), for one week intervals (original claim 10), and for first administration at 7 days old (original claim 8).

With regard to the "other than BCG" limitation (1),

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[3] Adams immunized with "phase I superconcentrate vaccine", with a total dose of "100,000,000,000 organisms".

limitation appears to be intended to excise prior art like that of Grange and Stanford (1990) cited at page 6, lines 11-14, and Harada (1990), cited at page 9, line 16 to page 10, line 4, and hence "described" by page 31, lines 9-18. Moreover, original claim 1 (which automatically has "description") recited "said one or more immunogens... optionally including at least one immunogen other than BCG". See also original claim 7.

Turning to limitation 3(a), we have already explained the basis for at least three dosings prior to 42 days after birth (original claim 13). With regard to 3(b), the basis for at least three dosings (not necessarily all prior to age 42 days) is in original claim 9 and for a maximum interval of about two weeks, at original claim 11. The ten immunogens in question are BCG (from original claim 1) plus those listed in original claim 4 (with the possibly inadvertent exception of hepatitis A). These are the ten pediatric immunogens listed on page 35, lines 24-26, and hence the ones for which the risk of inherent anticipation was greatest.

5. Enablement

At the outset, we would like to point out that the claims at issue are essentially parallel in scope to those granted in USP 5,728,385 and USP 5,728,283. These patents allowed claims which generically recited administering "immunogens" to "mammals". Those patents are presumptively valid under 35 USC §282. Moreover, the actions of the prior examiner in those cases is entitled to full faith and credit. Hence, we believe that the question of whether to maintain the instant enablement rejection should be reviewed by the Group Director.

5.1. The Examiner states in section 4(a) of the office action that

> Applicant argues that the specification is enabled for the broad scope of the claims because anthrax, plague and DT were shown to favorably affect diabetes and further argues that anthrax and DPT are very different. Applicant, however, does not elucidate what

> the significant differences are between anthrax and DPT (the examiner has assumed that "DT" is diphtheria/tetanus and that "DPT" is diphtheria/pertussis/tetanus). What the disclosure has shown is a reduction in the incidence of diabetes in a mouse model by administration of one or more of five bacterial immunogens (*Bacillus anthracis, Yersinia pestis, Corynebacterium diphtheriae, Bordetella pertussis, and Clostridium tetani*). This effect appears to be amplified when two or more of these antigens are administered together. The immunogens as claimed include a myriad of different viral antigens, as well as bacterial antigens. Applicant has not demonstrated the same effect for viral immunogens absent bacterial proteins and lipopolysaccharides that has been demonstrated for the described bacterial antigens.

The Examiner appears to assume that all of the bacterial vaccines mentioned contain LPS. Presumably, this is important because a viral coat would not contain LPS. However, at least the DT vaccine contains protein toxoids, without significant amounts of LPS, and hence is akin --in the sense that it presents just proteins to the immune system-- to a viral vaccine.

The immune system does not treat viral proteins any differently than it does bacterial proteins. That is why both viral and bacterial vaccines of at least partially proteinaceous character are known in the art.

It is not up to Applicant to elaborate upon the exact antigenic differences among plague, anthrax, diphtheria, pertussis and tetanus. It is up to the Examiner to prove, if he can, that these vaccines are so similar that Applicant's success with these vaccines is not properly extrapolated to vaccines based on other immunogens. Nonetheless, we wish to point out the separate classifications of the source organisms in the art:

anthrax (Bacillus anthracis)
plague (Yersina pestis)
diphtheria (Corynebacterium diphtheriae)
pertussis (Bordetella pertussis)

tetanus (Clostridium tetani)

Anthrax and tetanus are in the family Bacillaceae, but plague is in the family Enterobacteriaceae, while diphtheria is in the Actinomycetes. The affiliation of Bordetella is uncertain, but these bacteria are strictly aerobic coccobacilli.

It would therefore be reasonable to expect that the divergence in antigenic makeup among the exemplified immunogens is substantial, in which case generic coverage of immunogens -- especially coupled with a functional limitation -- is justified.

Besides the variety of bacterial immunogens which have been shown to reduce the incidence of diabetes, several viral immunogens have also been shown to have this effect.

The efficacy of a smallpox vaccine, administered at birth, has been established by epidemiological evidence. See Spec., pages 97-99.

More recently, the applicant has shown that a hepatitis B virus vaccine, administered on days 3 and 28 from birth, significantly protected NOD mice from the development of diabetes (see enclosed Declaration).

5.2. The Examiner discounts (OA §4(b)) the relevance of the BCG epidemiological data because BCG contains "a known tolerogen, heat shock protein".

The epidemiological data related to administration of a live BCG (a whole bacterium), rather than of a purified heat shock protein. The subject was thus immunized with thousands of different membrane and intracellular proteins native to BCG. One of these may well have been heat shock protein, but there were certainly many others. Regardless of whether heat shock protein was functioning as an immunogen or a tolerogen, at least some of the proteins of the administered BCG preparation must have been functioning as immunogens because the preparation was administered as a vaccine, i.e., to elicit a specific immune response protective against tuberculosis.

Applicant discovered that it is the timing of the administration that determines whether an immunogen increases or

decreases the risk of developing autoimmunity. Based on the epidemiological data in question, it appears that early administration of BCG reduces incidence of diabetes, while late administration increases it. See specification Table I on pp. 101-102, and page 91, lines 4-6 and 8-11.

5.3. With regard to the other epidemiological data, the Examiner considers it inconclusive for the reasons stated in section 4(b). However, the Examiner's objections apply to any epidemiological study, and In re Irons held that use of "historical controls" is acceptable. Moreover, the epidemiological data does not stand alone.

While we have not established a mode of action (OA sec. 3(e)), the existence of a plausible mode of action renders the asserted utility more believable, and hence is legally relevant.

Moreover, the examiner errs on both scientific and ethical grounds in attempting to exclude historical and epidemiological data. These types of studies are the basis for pharmacotoxicology studies. It is unethical to do prospective studies to prove a drug can injure children, and hence it is not feasible or allowed to do such studies. Dr. Classen's epidemiology data has been published in many different journals and reviewed by editorial staff and scientific peers. Dr. Classen's smallpox data has been accepted for publication in the journal Autoimmunity. The BCG data been published in Diabetologia (39:500-501, 1996), Diabetes Care (20:1799-1800, 1997) and Infectious Diseases in Clinical Practice (6:449-454, 1997). Supporting data for the BCG includes a cohort study from Sweden (Diabetologia 39:500-501, 1996) and Germany (Diabetes Care 20:1799-1800, 1997).

5.4. In OA §4(c), the Examiner argues that preventing autoimmune diseases is highly unpredictable.

It is well accepted that immune suppressants like corticosteriods can suppress most if not all autoimmune diseases. It is also accepted that immune stimulants like interferons can exacerbate almost all autoimmune diseases. The PDR gives

specific contraindication not to give interferons to patients with autoimmune disease (PDR (1999) on Roferon). Vaccines induce interferons and would be expected to increase the risk of autoimmunity. Immune stimulation is a common pathway for exacerbating autoimmunity. A second common pathway for induction of autoimmune diseases is through vertical transmission of viruses. Interferon release following immune stimulation with vaccines would expect to prevent this (see below).

It follows from the general effects of immune suppressants and immune stimulants on autoimmune diseases that there are common mechanisms at work.

5.5. It appears from OA §4(d) that the Examiner overlooks (sec. 4(d)) the relevance of the Classen declaration. The antidiabetic effect is not a specific immune response to a diabetes-associated autoantigens, because, e.g., diphtheria and tetanus are not known to cross-react with such an antigen. If the effect is not a specific immune response, it is reasonable to expect that it can be achieved with many different antigens.

5.6. While we have not <u>established</u> a mode of action (OA sec. 3(e)), the existence of a <u>plausible</u> mode of action renders the asserted utility more believable, and hence is legally relevant.

5.7. The Examiner has questioned the extrapolation from rodents to humans "because of the criticality of the age of administration of the immunogens and the difference in maturation rates between rodents and humans" (OA §4(i)).

The issue of maturation rates is discussed in the specification. It is not the overall maturation rate which is important, just the rate of maturation of the immune system.

The specification states at page 27, lines 15-23:

> The immune systems of mice and men mature at comparable rates, with both species capable of mounting immune responses to vaccine antigens by the time the recipients are several months old. A comparison of the experimental and epidemiological examples in this specification supports this conclusion.

> Subtle differences in the rates of development of the immune systems of mice and humans may be detected however using a broad range of assays including in vivo assays, in vitro assays, in vitro assays and phenotypic cell assays.

It then discusses the appropriate assays in detail, at page 27, line 24 to page 29, line 12, and concludes at page 29, lines 13-19:

> The present invention therefore can include administration of the immunogens to humans when said humans' immune systems are in a state of maturation and responsiveness comparable to that of mice or rats at the times indicated above, in such circumstances as it would be less effective to administer those immunogens to humans at the same chronological ages as they were administered to mice or rats.

In view of the issue raised by the Examiner, Applicants are filing a supplemental amendment adding new claims which refer to first administration to a human subject when the immune system of that subject is at a state of maturation comparable to that achieved prior to 42 days after birth in a mouse or rat.

It is becoming clear that vertically transmitted viral infections are associated with an increased risk of diabetes and other autoimmune disease. Mothers become infected with viruses such as the enterovirus and rubella virus when they are pregnant leading to an infection of the newborn and an increased risk of autoimmunity including IDDM later in life. Vertically transmitted viruses have been shown to induce diabetes in both mice and humans. For mice, see Gaskins, et al., J. Clin. Invest., 90:2220-7 (1992) (retrovirus in NOD mice); Suenaga and Brown, Diabetes, 37:1722 (1988) (abstract); Serreze, et al. Diabetes, 37:351-8 (1988). In humans, see Dahlquist, et al., Diabetes Care, 22:364-65 (1999) ("enterovirus RNA has been detected early in pregnancy in mothers of children who later become diabetic in a higher frequency than that found in mothers of control subjects").

It has been shown that immunization of newborns with

vaccines after birth can protect against vertical transmission of viruses such as hepatitis B. Administration of antiviral drugs after birth can prevent vertical transmission of the HIV (AIDs) virus to newborns.

It is also known that administration of interferons will stop the replication and spread of viruses. It would be expected that giving an immune stimulant like a vaccine which cause interferon release would impede vertical transmission of viruses and thereby decrease the risk of IDDM.

Vertical transmission of viruses in NOD mice has also been implicated as a cause of diabetes in mice and would explain why early immunization is effective in these animals. Viral transmissions are similar in mice and men so the comparison of age is a moot point.

5.8. The question of coverage of future vaccines (4(j)) is one considered and resolved during the prosecution of the parent application, Serial No. 08/104,529, now USP 5,728,385. The Examiner of the parent application said that Applicant could not specifically claim immunization against HIV, but could claim immunogens, implicitly including HIV, generically. That permitted a compromise, whereby Applicant received generic coverage of various immunogens, including HIV, but did not specifically claim HIV. The present Examiner would apparently limit Applicant only to those antigens already in use as vaccines.

That position is entirely without justification when the claimed purpose of the immunogen is merely to protect against diabetes. There was no known relationship between diabetes and anthrax, plague, diphtheria, pertussis or tetanus. Hence, the antidiabetic effect plainly was not a specific response, and hence there is no reason to believe that an HIV immunogen would not work just as well.

In section 4(f), the Examiner cites the intended use from the preamble of kit claim 59 ("for use to protect a mammal against an infectious disease). The Examiner completely ignores

the very different preamble of claim 27 ("to reduce the incidence or severity of a chronic immune-mediated disorder"). While we agree that a particular immunogen may have both these effects, the application does not require that it be used to immunize against an infectious disease at all. Clearly, the "nonpediatric immunogens" of pp. 35-36 would be administered pediatrically in the United States principally to protect against juvenile diabetes, etc, and not against an infectious disease.

5.9. In section 13 of the office action, the Examiner questioned whether the immunogenic compositions can "protect" against an infectious disease.

The Examiner construes "protect" as requiring absolute prevention of the infectious disease. When we amended claim 59, we pointed out that "protect" means, "confers a beneficial clinical effect, see page 47, lines 7-10. Protection is a matter of degree, see page 72, lines 15 and 21".

The Examiner admits that applicant may define terms for greater clarity, but is of the opinion that "protection implies an absolute, not a matter of degree", and that this implication is so strong that applicant's definition would be "repugnant to the usual meaning of the term".

While we agree with the Examiner that In re Hill defines the proper legal standard, we do not believe that he has made out the necessary prima facie case as to the accepted meaning of "protection".

In Webster's New Twentieth Century Dictionary, Unabridged, Second Edition, page 476, the writers give the example, "A fortress is defended by its guns, and protected by its walls". But history gives ample instances of fortresses whose walls were scaled or knocked down by an enemy, so the protection provided by those walls plainly is not absolute.

It is clear that in the vaccinological literature, the term "protection" is used so as to encompass partial protection. Thus, in Halsey (1985), cited by the Examiner, the first sentence of the introduction reads, "Infants should receive

immunization... in order to be protected against the natural diseases...." At page 1163, under "conclusions", Halsey speaks of a means of "improving protection", which would be a meaningless concept if "protection" were necessarily all or nothing.

Madore, also cited by the Examiner, states on page 335 that antibodies to a particular capsular polysaccharide "confer protection from" H. influenzae type B. While more than 90% of the infants responded, the number was still less than 100%.

Claim 1 of Tendler, USP 5,730,984 is directed to "An immunogenic composition able to confer at least partial protection against infection with pathogenic helminths".

Claim 1 of Knapp, USP 5,393,523 covers "a method of inducing partial immunological protection against P. falciparum blood stage infection in a patients".

The term "partial protection" would not have been used by these inventors, or accepted by the PTO, if the only accepted meaning of "protection" were absolute protection.

Respectfully submitted,

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Enclosure
-Declaration
-Dalquist
-Gaskins
-Suenaga (abstract)
-Serreze
IPC:lms
f:\user19\wp\a-c\cla651us.aaf